

PATENT

Our Docket: P-HP 3808

#12/12
2/27/03
H. Meier

TECH CENTER 1600/2900

FEB 25 2003

RECEIVED

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of) Group Art Unit: 1621
Watson-Straughan et al.)
Serial No: 09/632,928) Examiner: S. Barts
Filed: August 4, 2000)
For: TRIAMINE DERIVATIVE)
MELANOCORTIN RECEPTOR)
LIGANDS AND METHODS)
OF USING SAME)

Commissioner for Patents
Washington, D.C. 20231

I hereby certify that this correspondence
is being deposited with the United States
Postal Service as first class mail in an
envelope addressed to: Commissioner for
Patents, Washington, D.C., 20231 on
February 12, 2003.

David I. Spolter
David I. Spolter, Reg. No. 36,933

February 12, 2003
Date

RESPONSE TO OFFICE ACTION

Responsive to the Office Action mailed August 13,
2002, entry of the following Amendments and Remarks is
respectfully requested. A response was initially due by
November 13, 2002. However, a petition for extension,
requesting an extension of three months, or until February
13, 2003, along with the corresponding extension fee, is
submitted herewith. Accordingly, this response is timely
filed.

02/21/2003 MN0HAMM1 00000092 09632928

01 FC:1201

168.00 OP

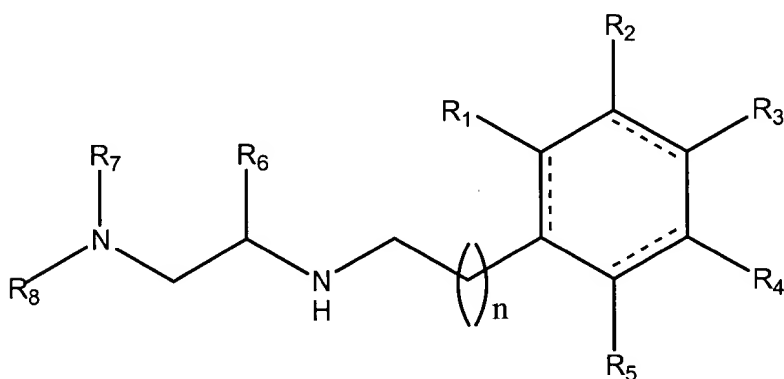
I. AMENDMENTS

Clean version

Please cancel claims 2 and 20 to 41 without prejudice.

Please amend the claims as follows:

1. (Amended) A compound of the formula:



wherein:

the dotted lines indicate that the depicted ring is selected from the group consisting of phenyl and cyclohexyl;

n is 0, 1 or 2;

al

R₁ to R₅ are, independently, selected from the group consisting of a hydrogen atom, halo, hydroxy, protected hydroxy, nitro, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₃ to C₇ cycloalkyl, C₃ to C₇ substituted cycloalkyl, C₅ to C₇ cycloalkenyl, C₅ to C₇ substituted cycloalkenyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C₁ to C₆ alkoxy, C₁ to C₆ substituted alkoxy, phenoxy, substituted phenoxy, C₁ to C₆ alkylthio, C₁ to C₆ substituted alkylthio, C₁ to C₆ alkylsulfonyl, C₁ to C₆ substituted alkylsulfonyl, phenylthio, substituted phenylthio, phenylsulfonyl, substituted phenylsulfonyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino; and when any one of adjacent position pairs R₁ and R₂, R₂ and R₃, and R₃ and R₄ and R₄ and R₅ together form a moiety selected from the group consisting of phenyl, substituted phenyl, heterocycle and substituted heterocycle, said moiety fused to the phenyl ring depicted in the above formula such that a bicyclic ring results;

R₆ is selected from the group consisting of a hydrogen atom, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₁₁ to C₁₆ naphthylalkyl and C₁₁ to C₁₆ substituted naphthylalkyl;

where R₇ is absent, R₈ together with the attached nitrogen depicted in the above formula form a substituted heterocycle or a substituted cyclic C₃ to C₇ heteroalkylene, wherein at least one of said substitution is the formula - D-E, wherein D may be absent or present and, if present, is

21

selected from the group consisting of C_1 to C_6 alkylene and C_1 to C_6 substituted alkylene; and E is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino group; and

where R_7 is selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl and C_1 to C_6 substituted alkyl, R_8 is the formula $X-CH-Y$, wherein the attached nitrogen depicted in the above formula is attached to the carbon atom of the formula $X-CH-Y$, and wherein X is selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, phenyl, substituted phenyl, naphthyl and substituted naphthyl, and Y is the formula $(CH_2)_n-Z$, wherein n is 1 to 6 and Z is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino;

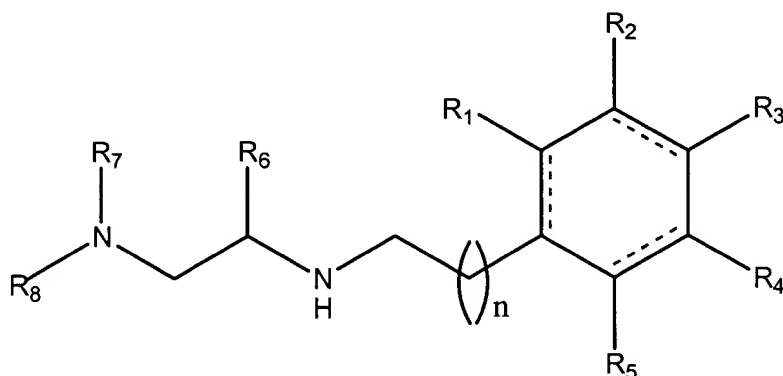
wherein, when a) the depicted ring is phenyl, and b) R_1 to R_5 and R_7 are each hydrogen and c) R_8 is the formula $X-CH-Y$, where X is benzyl and Y is $-CH_2$ -amino, then R_6 is not benzyl; or

a pharmaceutically-acceptable salt thereof.

OK

Please add the following claims:

43. (New) A compound of the formula:



wherein:

the dotted lines indicate that the depicted ring is selected from the group consisting of phenyl and cyclohexyl;

n is 0, 1 or 2;

R₁ to R₅ are, independently, selected from the group consisting of a hydrogen atom, halo, hydroxy, protected hydroxy, nitro, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₃ to C₇ cycloalkyl, C₃ to C₇ substituted cycloalkyl, C₅ to C₇ cycloalkenyl, C₅ to C₇ substituted cycloalkenyl, phenyl,

B2

substituted phenyl, naphthyl, substituted naphthyl, C₁ to C₆ alkoxy, C₁ to C₆ substituted alkoxy, phenoxy, substituted phenoxy, C₁ to C₆ alkylthio, C₁ to C₆ substituted alkylthio, C₁ to C₆ alkylsulfonyl, C₁ to C₆ substituted alkylsulfonyl, phenylthio, substituted phenylthio, phenylsulfonyl, substituted phenylsulfonyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino; and when any one of adjacent position pairs R₁ and R₂, R₂ and R₃, and R₃ and R₄ and R₄ and R₅ together form a moiety selected from the group consisting of phenyl, substituted phenyl, heterocycle and substituted heterocycle, said moiety fused to the phenyl ring depicted in the above formula such that a bicyclic ring results;

R₆ is selected from the group consisting of C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₁₁ to C₁₆ naphthylalkyl and C₁₁ to C₁₆ substituted naphthylalkyl;

where R₇ is absent, R₈ together with the attached nitrogen depicted in the above formula form a substituted heterocycle or a substituted cyclic C₃ to C₇ heteroalkylene, wherein at least one of said substitution is the formula - D-E, wherein D may be absent or present and, if present, is selected from the group consisting of C₁ to C₆ alkylene and C₁ to C₆ substituted alkylene; and E is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino group; and

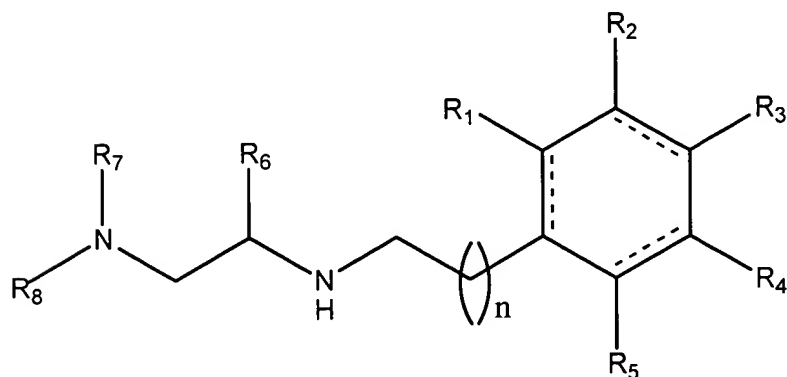
62

where R_7 is selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl and C_1 to C_6 substituted alkyl, R_8 is the formula $X-CH-Y$, wherein the attached nitrogen depicted in the above formula is attached to the carbon atom of the formula $X-CH-Y$, and wherein X is selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, phenyl, substituted phenyl, naphthyl and substituted naphthyl, and Y is the formula $-(CH_2)_n-Z$, wherein n is 1 to 6 and Z is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino;

wherein, when a) the depicted ring is phenyl, and b) R₁ to R₅ and R₇ are each hydrogen and c) R₈ is the formula X-CH-Y, where X is benzyl and Y is -CH₂-amino, then R₆ is not benzyl; or

a pharmaceutically-acceptable salt thereof.

44. (New) A compound of the formula:



2

wherein:

the dotted lines indicate that the depicted ring is selected from the group consisting of phenyl and cyclohexyl;

n is 0, 1 or 2;

R₁ to R₅ are, independently, selected from the group consisting of a hydrogen atom, halo, hydroxy, protected hydroxy, nitro, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₃ to C₇ cycloalkyl, C₃ to C₇ substituted cycloalkyl, C₅ to C₇ cycloalkenyl, C₅ to C₇ substituted cycloalkenyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C₁ to C₆ alkoxy, C₁ to C₆ substituted alkoxy, phenoxy, substituted phenoxy, C₁ to C₆ alkylthio, C₁ to C₆ substituted alkylthio, C₁ to C₆ alkylsulfonyl, C₁ to C₆ substituted alkylsulfonyl, phenylthio, substituted phenylthio, phenylsulfonyl, substituted phenylsulfonyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino; and when any one of adjacent position pairs R₁ and R₂, R₂ and R₃, and R₃ and R₄ and R₄ and R₅ together form a moiety selected from the group consisting of phenyl, substituted phenyl, heterocycle and substituted heterocycle, said moiety fused to the phenyl ring depicted in the above formula such that a bicyclic ring results;

R₆ is selected from the group consisting of a hydrogen atom, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂

22

phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₁₁ to C₁₆ naphthylalkyl and C₁₁ to C₁₆ substituted naphthylalkyl;

where R₇ is absent, R₈ together with the attached nitrogen depicted in the above formula form a substituted heterocycle or a substituted cyclic C₃ to C₇ heteroalkylene, wherein at least one of said substitution is the formula - D-E, wherein D may be absent or present and, if present, is selected from the group consisting of C₁ to C₆ alkylene and C₁ to C₆ substituted alkylene; and E is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino group; and

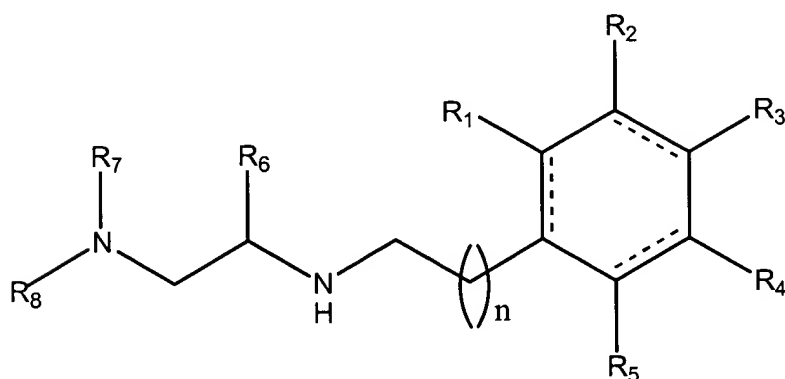
where R₇ is selected from the group consisting of a hydrogen atom, C₁ to C₆ alkyl and C₁ to C₆ substituted alkyl, R₈ is the formula X-CH-Y, wherein the attached nitrogen depicted in the above formula is attached to the carbon atom of the formula X-CH-Y, and wherein X is selected from the group consisting of a C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, phenyl, substituted phenyl, naphthyl and substituted naphthyl, and Y is the formula -(CH₂)_n-Z, wherein n is 1 to 6 and Z is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino;

wherein, when a) the depicted ring is phenyl, and b) R₁ to R₅ and R₇ are each hydrogen and c) R₈ is the formula X-CH-Y,

where X is benzyl and Y is -CH₂-amino, then R₆ is not benzyl; or

a pharmaceutically-acceptable salt thereof.

45. (New) A compound of the formula:



wherein:

the dotted lines indicate that the depicted ring is selected from the group consisting of phenyl and cyclohexyl;

n is 0, 1 or 2;

R₁, R₂, R₄ and R₅ are, independently, selected from the group consisting of a hydrogen atom, halo, hydroxy, protected hydroxy, nitro, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₃ to C₇ cycloalkyl, C₃ to C₇ substituted cycloalkyl, C₅ to C₇

62

cycloalkenyl, C₅ to C₇ substituted cycloalkenyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C₁ to C₆ alkoxy, C₁ to C₆ substituted alkoxy, phenoxy, substituted phenoxy, C₁ to C₆ alkylthio, C₁ to C₆ substituted alkylthio, C₁ to C₆ alkylsulfonyl, C₁ to C₆ substituted alkylsulfonyl, phenylthio, substituted phenylthio, phenylsulfonyl, substituted phenylsulfonyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino; R₃ is selected from the group consisting of a hydrogen atom, halo, hydroxy, protected hydroxy, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₃ to C₇ cycloalkyl, C₃ to C₇ substituted cycloalkyl, C₅ to C₇ cycloalkenyl, C₅ to C₇ substituted cycloalkenyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C₁ to C₆ alkoxy, C₁ to C₆ substituted alkoxy, phenoxy, substituted phenoxy, C₁ to C₆ alkylthio, C₁ to C₆ substituted alkylthio, C₁ to C₆ alkylsulfonyl, C₁ to C₆ substituted alkylsulfonyl, phenylthio, substituted phenylthio, phenylsulfonyl, substituted phenylsulfonyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino; and when any one of adjacent position pairs R₁ and R₂, R₂ and R₃, and R₃ and R₄ and R₄ and R₅ together form a moiety selected from the group consisting of phenyl, substituted phenyl, heterocycle and substituted heterocycle, said moiety fused to the phenyl ring depicted in the above formula such that a bicyclic ring results;

R₆ is selected from the group consisting of a hydrogen atom, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂

B2

phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₁₁ to C₁₆ naphthylalkyl and C₁₁ to C₁₆ substituted naphthylalkyl;


where R₇ is absent, R₈ together with the attached nitrogen depicted in the above formula form a substituted heterocycle or a substituted cyclic C₃ to C₇ heteroalkylene, wherein at least one of said substitution is the formula - D-E, wherein D may be absent or present and, if present, is selected from the group consisting of C₁ to C₆ alkylene and C₁ to C₆ substituted alkylene; and E is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino group; and

where R₇ is selected from the group consisting of a hydrogen atom, C₁ to C₆ alkyl and C₁ to C₆ substituted alkyl, R₈ is the formula X-CH-Y, wherein the attached nitrogen depicted in the above formula is attached to the carbon atom of the formula X-CH-Y, and wherein X is selected from the group consisting of a hydrogen atom, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, phenyl, substituted phenyl, naphthyl and substituted naphthyl, and Y is the formula - (CH₂)_n-Z, wherein n is 1 to 6 and Z is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino; or

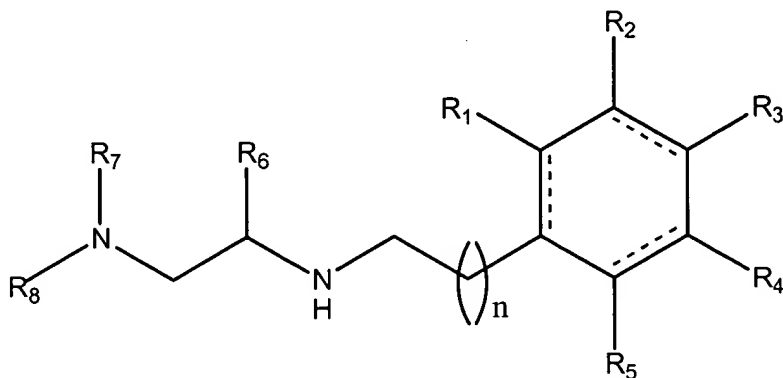
a pharmaceutically-acceptable salt thereof.

B2

46. (New) The compound of claim 45, wherein:
R₁ to R₅ are, independently, selected from the group
consisting of a hydrogen atom, halo, hydroxy, protected
hydroxy, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂
phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₃ to C₇
cycloalkyl, C₃ to C₇ substituted cycloalkyl, C₅ to C₇
cycloalkenyl, C₅ to C₇ substituted cycloalkenyl, phenyl,
substituted phenyl, naphthyl, substituted naphthyl, C₁ to C₆
alkoxy, C₁ to C₆ substituted alkoxy, phenoxy, substituted
phenoxy, C₁ to C₆ alkylthio, C₁ to C₆ substituted alkylthio,
C₁ to C₆ alkylsulfonyl, C₁ to C₆ substituted alkylsulfonyl,
phenylthio, substituted phenylthio, phenylsulfonyl,
substituted phenylsulfonyl, amino, protected amino,
(monosubstituted)amino, protected (monosubstituted)amino
and (disubstituted)amino; and when any one of adjacent
position pairs R₁ and R₂, R₂ and R₃, and R₃ and R₄ and R₄ and
R₅ together form a moiety selected from the group consisting
of phenyl, substituted phenyl, heterocycle and substituted
heterocycle, said moiety fused to the phenyl ring depicted
in the above formula such that a bicyclic ring results.



47. (New) A compound of the formula:



wherein:

the dotted lines indicate that the depicted ring is selected from the group consisting of phenyl and cyclohexyl;

n is 1 or 2;

R₁ to R₅ are, independently, selected from the group consisting of a hydrogen atom, halo, hydroxy, protected hydroxy, nitro, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₃ to C₇ cycloalkyl, C₃ to C₇ substituted cycloalkyl, C₅ to C₇ cycloalkenyl, C₅ to C₇ substituted cycloalkenyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C₁ to C₆ alkoxy, C₁ to C₆ substituted alkoxy, phenoxy, substituted


62

phenoxy, C₁ to C₆ alkylthio, C₁ to C₆ substituted alkylthio, C₁ to C₆ alkylsulfonyl, C₁ to C₆ substituted alkylsulfonyl, phenylthio, substituted phenylthio, phenylsulfonyl, substituted phenylsulfonyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino; and when any one of adjacent position pairs R₁ and R₂, R₂ and R₃, and R₃ and R₄ and R₄ and R₅ together form a moiety selected from the group consisting of phenyl, substituted phenyl, heterocycle and substituted heterocycle, said moiety fused to the phenyl ring depicted in the above formula such that a bicyclic ring results;

R₆ is selected from the group consisting of a hydrogen atom, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, C₁₁ to C₁₆ naphthylalkyl and C₁₁ to C₁₆ substituted naphthylalkyl;

where R₇ is absent, R₈ together with the attached nitrogen depicted in the above formula form a substituted heterocycle or a substituted cyclic C₃ to C₇ heteroalkylene, wherein at least one of said substitution is the formula - D-E, wherein D may be absent or present and, if present, is selected from the group consisting of C₁ to C₆ alkylene and C₁ to C₆ substituted alkylene; and E is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino group; and

where R₇ is selected from the group consisting of a hydrogen atom, C₁ to C₆ alkyl and C₁ to C₆ substituted alkyl, R₈ is



the formula X-CH-Y, wherein the attached nitrogen depicted in the above formula is attached to the carbon atom of the formula X-CH-Y, and wherein X is selected from the group consisting of a hydrogen atom, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl, phenyl, substituted phenyl, naphthyl and substituted naphthyl, and Y is the formula - (CH₂)_n-Z, wherein n is 1 to 6 and Z is selected from the group consisting of amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino and (disubstituted)amino;

wherein, when a) the depicted ring is phenyl, and b) R₁ to R₅ and R₇ are each hydrogen and c) R₈ is the formula X-CH-Y, where X is benzyl and Y is -CH₂-amino, then R₆ is not benzyl; or

a pharmaceutically-acceptable salt thereof.

II. REMARKS

Applicants wish to thank the Examiner for kindly indicating that claims 15 to 19 are allowable subject matter.

Before the amendments made herein, claims 1 to 42 were pending. Claims 2 and 20 to 41 have been canceled herein without prejudice. Claims 43 to 47 have been added herein. Accordingly, after entry of the amendments made herein, claims 1, 3 to 19 and 42 to 47 will be pending.